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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,782	09/08/2003	Phillip Arcangel	PP-19199.002	7355

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EXAMINER	
SALVOZA, M FRANCO G	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/658,782	ARCANGEL ET AL.
	Examiner	Art Unit
	M. Franco Salvoza	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6-16,19 and 22-34* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 7-14, 19, 23-30* is/are rejected.

7)☒ Claim(s) *6,15,16,22,31 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Salvoza.

2. Claims 3, 6-16, 19 and 22-32 were pending as of the last Office Action.

Election/Restrictions

New claims 33 and 34 added in the previous response were withdrawn from consideration as being directed to a nonelected invention. Applicant argues that an examination of claims 33 and 34 along with those pending in the application would not impose a serious burden on the Examiner.

Applicant's arguments are considered and found unpersuasive. Claims 33 and 34 recite MEFAs 13 and 13.1, otherwise drawn to MEFA 12 with specific modifications. The claims do not include the limitations of previously searched subject matter deemed allowable whose modifications are beyond the scope of that previously searched.

Claims 3, 6-16, 19 and 22-32 are pending and under consideration.

Responses to Applicant's Arguments

WITHDRAWN

Claims 3, 7-8, 10-14, 19, 23-24, 26-30 were rejected under 103(a) as being unpatentable over Chien et al. in view of Seidel et al. and Choo et al.

Applicant argues that Chien et al. teaches a chimeric HCV polypeptide termed "MEFA-6" which includes several HCV epitopes but does not contain a consensus sequence from the E2 hypervariable region spanning amino acids 390-410 as claimed after amendment, rather the E2 epitope present in MEFA-6 includes the amino acid sequence found at positions 405-444. Furthermore, there is no teaching or suggestion to provide a multiple epitope fusion antigen as claimed that includes a consensus sequence from the E2 hypervariable region.

Applicant also argues that Seidel et al. fails to teach both a MEFA and an NS3/4a antigen in an assay as claimed in the current application, and Choo et al. provides the sequence of the HCV-1 polyprotein, which includes over 3000 amino acids. Although Choo et al.'s full length sequence includes an internal sequence homologous to the NS3/4a epitope, there is no suggestion to use this or any other portion of the polyprotein in assays as claimed.

Applicant's arguments are considered and found persuasive, since Chien et al.-1 does not teach the E2 hypervariable region spanning amino acids 390-410.

However, applicant's argument that Choo et al.'s full length sequence includes an internal sequence homologous to the NS3/4a epitope but lacks any suggestion to use it is not persuasive. The claim recites HCV antigen "comprising a conformational epitope, wherein the NS3/4a antigen has an amino acid sequence with at least 80% sequence identity." Choo et al.'s over 3000 amino acid full length sequence *comprises* (emphasis added) the internal sequence homologous to the NS3/4a epitope.

This rejection is withdrawn because of the assertion that Chien et al.-1 fails to teach the E2 hypervariable region.

Claims 9 and 25 were rejected under 103(a) as being unpatentable over Chien-1 in view of Seidel et al. and Choo et al. as applied to claims 3, 7-8, 10-14, 19, 23-24, and 26-30 and further in view of Chien-2.

Claims 9 and 25 are directed to an assay method using a MEFA with the full length helicase region of NS3, spanning amino acids 1193-1657.

Applicant argues that the combination of Chien-1 in view of Seidel and Choo is not believed to render the base claims from which claims 9 and 25 depend obvious; the addition of Chien-2 does not cure the defects of the primary and secondary references; and the Office's assessment of Chien-2 is in error since Chien's chimeric antigen included only 266 amino acids, while the full length helicase domain as claimed in claims 9 and 25 includes 465 amino acids and is longer, and Chien-2 does not teach the full length helicase-region of NS3.

Applicant's arguments are considered and found persuasive and the rejection is withdrawn. As cited previously, Chien-1 from which the base claim rests does not teach the use of the E2 hypervariable region.

However, Chien-2 teaches that the c33c polypeptide appears to encode both a viral protease and a helicase" (column 1 p. 10012). Thus, Chien-2 suggests the use of helicase epitopes and the importance of the inclusion of antigenic determinants from the helicase region but the shorter helicase as recited on page 10011 at line 8 is sufficient, absent a showing of unexpected results for the amino acids that are not included.

Claims 3, 7-14, 19 and 23-30 were rejected under 103(a) as being unpatentable over Chien-2 in view of Seidel et al. and Choo et al.

Applicant argues that as shown in Figure 1 of Chien 2, the C25 chimeric polypeptide does not contain an epitope from E2 and does not teach the use of a consensus sequence from the E2 hypervariable region and there is no disclosure of SEQ ID NO:2; Choo et al. only pertains to the full-length HCV polyprotein and does not delineate regions; the Office is engaging in improper hindsight reconstruction.

Applicant's arguments are considered and found persuasive. This rejection is withdrawn because of the assertion that Chien et al.-2 fails to teach the E2 hypervariable region.

Response to Applicant's Arguments - MAINTAINED

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 7-8, 10-14, 19, 23-24 and 26-30 were rejected under 103(a) as being unpatentable over Valenzuela et al. (U.S. Patent 6,428,792) in view of Seidel and Choo. The Office argued that Valenzuela taught MEFA-2, MEFA-5, and MEFA-6 that included epitopes from the NS3/NS4a region; Seidel teaches a double antigen bridge test and Choo et al. teaches a sequence 99.5% identical to SEQ ID NO: 2.

Applicant argues that Valenzuela et al., which fails to describe a double antigen bridge assay method, does not speak to the use of a conformational epitope of NS3/4a; Seidel et al. fails to teach or suggest the use of any MEFA or both a MEFA and a NS3/4a antigen; Choo et al. fails

to describe an assay using both a MEFA and an NS3/4a antigen and the polyprotein in Choo et al. includes over 3000 amino acids and lacks any suggestion or teaching as to the boundaries of particular HCV regions of the polyprotein and states that the identities of the regions had not yet been determined; Choo fails to provide any guidance with respect to the use of a NS3/4a epitope and provides no suggestion or motivation to use this particular unidentified epitope. Finally, the rejection was made impermissibly using hindsight reconstruction.

Applicant's arguments are considered and found unpersuasive. Valenzuela et al. does teach the use of MEFA chimeric polypeptides that included epitopes from NS3/NS4a as a way to bind HCV-specific antibody, and Seidel et al. teaches a format (double bridge antigen assay) for using HCV antigens from NS3 that results in increased sensitivity and specificity. One of ordinary skill in the art would be motivated to combine the teachings of the two to in order to create an immunological test for the detection of HCV antibodies with increased sensitivity and specificity. This is not a hindsight reconstruction, as argued by applicant, rather that one of ordinary skill in the art would be motivated to combine the teachings to increase sensitivity and specificity within the context for immunological tests for HCV-specific antibodies to NS3. Furthermore, as cited previously, Choo et al.'s sequence that is 99.5% identical to applicant's SEQ ID NO: 2 applies since the claims recite that the antigen comprise a conformational epitope, wherein the NS3/4a antigen has an amino acid sequence with at least 80% sequence identity to SEQ ID NO: 2. Choo et al's sequence, which is 99.5% identical, comprises smaller portions of conformational epitope.

Claims 9 and 25 were rejected under 103(a) as being unpatentable over Valenzuela in vew of Seidel et al. and Choo et al. as applied to claims 3, 7-8, 10-14, 19, 23-24 and 26-30 above and further in view of Chien-2.

Applicant argues that Valenzuela et al. in view of Seidel et al. and Choo et al. falls for the reasons described previously, and Chien falls for the reasons described previously as well; the helicase domain recited spans 465 amino acids, almost 200 amino acids more than the portion of the helicase domain used in Chien-2 and does not explain which amino acids of NS3 were used; the rejection is premised on hindsight reconstruction.

Applicant's arguments are considered and found unpersuasive. Chien-2 teaches that the c33c polypeptide appears to encode both a viral protease and a helicase" (column 1 p. 10012). Thus, Chien-2 suggests the use of helicase epitopes and the importance of the inclusion of antigenic determinants from the helicase region but the shorter helicase as recited on page 10011 at line 8 is sufficient, absent a showing of unexpected results for the amino acids that are not included.

Double Patenting

WITHDRAWN

The claims were rejected under obviousness-type double patenting over U.S. Patent Nos. 6,428,792; 6,632,601; 6,797,809; 6,630,298; and U.S. Application Nos. 10/643,853; 10/174,652; and 10/899,716.

Applicants have submitted a terminal disclaimer over U.S. Patents 6,632,601 and 6,630,298.

Claims 3, 6-16, 19 and 22-32 were rejected under obviousness-type double patenting as being unpatentable over claims 1-58 of copending application 10/643,853.

Applicant argues that the claims in '853 are directed to polynucleotides, vectors, host cells and methods of recombinant production, but do not pertain to immunoassays as claimed in the instant application and that the polynucleotides and immunoassays are separately patentable inventions. Moreover that there was a restriction requirement in the parent 09/881,239 application that recognized that polynucleotides, vectors, host cells and methods of production are separate and distinct from immunoassay methods.

Applicant's arguments are considered and found persuasive. The rejection is withdrawn.

Claims 3, 6-16, 19 and 22-32 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 29-47 of U.S. Application 10/899,715.

Applicant argues that the claims pertain to polynucleotides, vectors, host cells and methods of recombinant production were restricted and considered patentably distinct from immunoassays in the original parent application.

Applicant's arguments are considered and found persuasive. The rejection is withdrawn.

Claims 3, 6-16, 19 and 22-32 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-49 of copending U.S. application 10/174,652.

Applicant requests the rejection be held in abeyance until allowable subject matter is indicated in either or both of the instant application or the '652 application, then will consider filing a terminal disclaimer.

Applicant's arguments are considered. The rejection will be held in abeyance until allowable subject matter is indicated or both of the instant application or the '652 application.

Caims 3, 6-16, 19 and 22-32 were rejected under the judicially created doctrine of obviousness type double patenting over claims 1-20 of U.S. Patent 6/428,792 and claims 1-4 of U.S. Patent No. 6,797,809.

Applicant argues that the claims are directed to MEFAs and not to immunodiagnostic methods; Patent Office views MEFAs and immunodiagnostic methods as separately patentable inventions.

Applicant's arguments are considered and found persuasive. The rejection is withdrawn.

Claim Rejections - 35 USC § 103

NEW

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 7, 8, 10-14, 19, 23, 24, 26, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien-1, Seidel et al., Choo et al. in view of Wang et al. (2000).

Claims 3 and 19 further recite the method of detecting HCV infection in a biological sample, said method comprising: said labeled MEFA comprising at least one epitope from the HCV NS3/4a region and a consensus sequence from the E2 hypervariable region spanning amino acids 390-410, numbered relative to the HCV-1 polyprotein sequence.

See the previous teachings of Chien-1, Seidel et al. and Choo et al.

Chien-1, Seidel et al. and Choo et al. do not teach the use of an E2 hypervariable consensus sequence spanning amino acids 390-410.

Wang et al. (abstract, 2000) teaches the use of multiple antigen peptide corresponding to the HCV hypervariable region 1 consensus sequence within E2/NS1 spanning amino acids 390-411 (which encompasses said 390-410 amino acid spanning region) as an hepatitis C antigenic epitope that elicited higher titer antibody and stronger immunogenic response.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the epitopes, assays and sequence of Chien-1, Seidel et al. and Choo et al. and the E2 hypervariable consensus sequence of Wang et al. because Wang et al. teaches the use of the hypervariable region 1 spanning amino acids 390-411 to bind higher titer antibody and improve immunogenicity, thus increasing assay sensitivity for HCV.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the epitopes, assays and sequence of Chien-1, Seidel et al. and Choo et al. and the E2 hypervariable consensus sequence of Wang et al. because because Chien-1, Seidel et al., Choo et al. and Wang et al. all teach the use of HCV immunogenic epitopes.

Therefore, the invention as a whole would have been prima facie obvious to one of

ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 9 and 25 are rejected under 103(a) as being unpatentable over Chien-1 in view of Seidel et al. and Choo et al. as applied to claims 3, 7-8, 10-14, 19, 23-24, and 26-30 and further in view of Chien-2 and Wang et al.

Claims 9 and 25 are directed to an assay method using a MEFA with the full length helicase region of NS3, spanning amino acids 1193-1657.

See the previous teachings of Chien-1, Seidel et al., Choo et al. and Chien-2.

Chien-1, Seidel et al., Choo et al. and Chien-2 do not teach the use of an E2 hypervariable consensus sequence spanning amino acids 390-410.

Wang et al. (abstract, 2000) teaches the use of multiple antigen peptide corresponding to the HCV hypervariable region 1 consensus sequence within E2/NS1 spanning amino acids 390-411 (which encompasses said 390-410 amino acid spanning region) as an hepatitis C antigenic epitope that elicited higher titer antibody and stronger immunogenic response.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the epitopes, assays and sequences of Chien-1, Seidel et al., Choo et al. and Chien-2 and the E2 hypervariable consensus sequence of Wang et al. because Wang et al. teaches the use of the hypervariable region 1 spanning amino acids 390-411 to bind higher titer antibody and improve immunogenicity, thus increasing assay sensitivity for HCV.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the epitopes, assays and sequence of Chien-1, Seidel et al., Choo et al. and Chien-2 and the E2 hypervariable consensus sequence of Wang et al.

because because Chien-1, Seidel et al., Choo et al., Chien-2 and Wang et al. all teach the use of HCV immunogenic epitopes.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 3, 7-14, 19 and 23-30 are rejected under 103(a) as being unpatentable over Chien-2, Seidel et al., Choo et al. in view of Wang et al.

The claims are drawn to a method of detecting hepatitis C virus infection using a MEFA wherein the MEFA comprises at least one epitope in common and a consensus sequence from the E2 hypervariable region spanning amino acids 390-410 and either the antigen or the MEFA isused as the solid support. Claims subsequent to claim 1 require that the MEFA and the antigen to possess at least one epitope from the NS3/4a region or a specific region of the NS3/4a region.

See the teachings of Chien-2, Seidel et al., Choo et al.

Chien-2, Seidel et al., Choo et al. do not teach the use of an E2 hypervariable consensus sequence spanning amino acids 390-410.

Wang et al. (abstract, 2000) teaches the use of multiple antigen peptide corresponding to the HCV hypervariable region 1 consensus sequence within E2/NS1 spanning amino acids 390-411 (which encompasses said 390-410 amino acid spanning region) as an hepatitis C antigenic epitope that elicited higher titer antibody and stronger immunogenic response.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the epitopes, assays and sequence of Chien-2, Seidel et al., and Choo et al.

and the E2 hypervariable consensus sequence of Wang et al. because Wang et al. teaches the use of the hypervariable region 1 spanning amino acids 390-411 to bind higher titer antibody and improve immunogenicity, thus increasing assay sensitivity for HCV.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the epitopes, assays and sequence of Chien-2, Seidel et al., Choo et al. and the E2 hypervariable consensus sequence of Wang et al. because because Chien-2, Seidel et al., Choo et al. and Wang et al. all teach the use of HCV immunogenic epitopes.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Franco Salvoza
Patent Examiner

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